§ 160.190 Storage and retrieval of records and data.

(a) All raw data, documentation, records, protocols, specimens, and final reports generated as a result of a study shall be retained. Specimens obtained from mutagenicity tests, specimens of soil, water, and plants, and wet specimens of blood, urine, feces, and biological fluids, do not need to be retained beyond quality assurance. Correspondence and other documents relating to interpretation and evaluation of data, other than those documents contained in the final report, also shall be retained.

* * * * *

(e) Material retained or referred to in the archives shall be indexed to permit expedient retrieval.

25. In § 160.195, by revising paragraph (c) and adding paragraph (i) to read as follows:

§ 160.195 Retention of records.

* * * * *

(c) Wet specimens, samples of test, control, or reference substances, and specially prepared material which are relatively fragile and differ markedly in stability and quality during storage, shall be retained only as long the quality of the preparation affords evaluation. Specimens obtained from mutagenicity tests, specimens of soil, water, and plants, and wet specimens of blood, urine, feces, biological fluids, do not need to be retained beyond quality assurance review. In no case shall retention be required for longer periods than those set forth in paragraph (b) of this section.

* * * * *

(i) Records required by this part may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records.

[FR Doc. 87-29511 Filed 12-24-87; 8:45 am]
BILLING CODE 6560-50-M

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40 CFR Part 792

[OPTS-46016; FRL-3245-6]

Toxic Substances Control Act (TSCA); Good Laboratory Practice Standards

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: EPA is proposing to amend the TSCA Good Laboratory Practice (GLP) Standards to incorporate many of the changes made by the Food and Drug Administration (FDA) to its GLP regulations and to expand the scope of the TSCA GLP standards to apply to testing conducted in the field under TSCA. EPA is proposing this amendment in order to ensure the quality and integrity of data generated from such studies.

DATE: Submit written comments on or before March 28, 1988.

ADDRESS: Submit written comments, identified by the document control number (OPTS-46016), in triplicate to: TSCA Public Information Office (TS-793), Office of Pesticides and Toxic Substances, Environmental Protection Agency, Rm. NE-G004, 401 M St., SW., Washington, DC 20460.

The public record supporting this action is available for inspection at the above address from 8 a.m. to 4 p.m., Monday through Friday, except legal holidays.

FOR FURTHER INFORMATION CONTACT: Edward A. Klein, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Rm. E-543, 401 M St., SW., Washington, DC 20460 (202) 554-1404.

SUPPLEMENTARY INFORMATION: Following is an index to the remainder of this preamble:

I. Introduction

A. Legal Authority

On November 29, 1983 (48 FR 53922), EPA promulgated the GLP standards under the authority of TSCA section 4 (90 Stat. 2006, 15 U.S.C. 2603). Section 4(a) of TSCA authorizes the EPA Administrator to require, by rule, that manufacturers (including importers) and processors of identified chemical substances and mixtures test such chemicals if certain findings are made. Section 4(b)(1) of TSCA specifies that each test rule shall include standards for the development of test data. These standards are defined in section 3(12) of TSCA to mean a prescription of—

(A) the—
(i) health and environmental effects, and
(ii) information relating to the toxicity, persistence, and other characteristics which affect health and the environment, for which test data for a chemical substance or mixture are to be developed and any analysis that is to be performed on such data, and

(B) to the extent necessary to assure that data respecting such effects and characteristics are reliable and adequate—
(i) the manner in which such data are to be developed,
(ii) the specification of any test protocol or methodology to be employed in the development of such data, and
(iii) such other requirements as are necessary to provide such assurance.

In summary, the specific authority to issue the GLP standards is provided by section 4(b)(1) of TSCA, which is further explained by the definitions in sections 3(12)(B)(i) and 3(12)(B)(iii).

In addition, the Agency also requires sponsors to utilize these GLP standards when conducting testing under TSCA section 4 testing consent agreements and will include provisions to adhere to these GLP standards in those agreements (see 40 CFR 790.60(a)(7)). Also, it is the Agency's policy that all data developed as a result of rules or orders under section 5 of TSCA should be in accordance with the GLP standards. If data developed under section 5 of TSCA are not generated in accordance with the GLP standards, the Agency may elect to consider such data insufficient to evaluate the health effects, environmental effects, and fate of the chemical.

B. Background

EPA originally published enforceable TSCA Good Laboratory Practice Standards in the **Federal Register** of November 29, 1983 (48 FR 53922), which were codified as 40 CFR Part 792. At the same time, EPA published GLP standards applicable to testing under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA, 48 FR 53963, 40 CFR Part 160). These regulations were promulgated in response to investigations by EPA and FDA during the mid-1970s which revealed that some studies submitted to the Agencies had not been conducted in accordance with acceptable laboratory practices. Some studies had been conducted so poorly that the resulting data could not be relied upon in EPA's regulatory decisionmaking process. For instance, some studies had been submitted which did not adhere to specified protocols, were conducted by underqualified personnel and supervisors, or were not adequately monitored by study sponsors. In some cases results were selectively reported, underreported, or fraudulently reported. In addition, it was discovered that some testing facilities displayed poor animal care procedures and inadequate recordkeeping techniques. The TSCA GLP standards specify minimum practices and

procedures which must be followed in order to ensure the quality and integrity of data submitted in accordance with TSCA section 4 requirements. The 1983 TSCA GLP standards also established a policy that persons should comply with the GLP standards when submitting data in response to rules and orders issued under section 5 of TSCA, and when submitting data to the Agency voluntarily.

When EPA published its final TSCA and FIFRA GLP standards in the **Federal Register** of November 29, 1983, the Agency sought to harmonize the requirements and language with those regulations promulgated by the FDA in the **Federal Register** of December 22, 1978 (43 FR 60013), and codified as 21 CFR Part 58. Differences between the two Agencies' current GLP regulations exist only to the extent necessary to reflect the Agencies different statutory responsibilities under TSCA, FIFRA, and the Federal Food, Drug, and Cosmetic Act (FFDCA). Similar to the FDA GLP regulations, the FIFRA and TSCA GLPs delineate standards for studies designed to determine the health effects of a test substance; however, the TSCA GLPs also contain provisions related to environmental testing (i.e., ecological effects and chemical fate).

Compliance with EPA's GLP regulations has been monitored through a program of laboratory inspections and study audits coordinated between EPA and FDA. Under an Interagency Agreement originating in 1978, FDA carries out inspections at laboratories which conduct health effects testing. EPA primarily performs laboratory inspections and data audits for environmental studies.

After a thorough review of its GLP regulations and compliance program, FDA concluded that some of the provisions of the GLPs needed to be clarified, amended, or deleted in order to reduce the regulatory burden on testing facilities. Accordingly, FDA proposed revisions to its GLP regulations in the **Federal Register** of October 24, 1984 (49 FR 43530), which were intended to simplify the regulation without compromising study integrity. FDA's proposed revision has recently been published as a final rule in the **Federal Register** of September 4, 1987 (52 FR 33768).

EPA agrees with FDA that many provisions of the GLP regulations can be streamlined without compromising the goals of the GLPs. Therefore, EPA is proposing to amend the TSCA GLP standards to incorporate many of the changes recently made by FDA to its GLP regulations. In addition, EPA is proposing to expand the scope of the TSCA GLPs to cover testing wherever it is conducted (e.g., field testing). In another notice in this **Federal Register** EPA is proposing similar changes to the FIFRA GLP standards.

C. Consistency With FDA GLP Regulations

It is EPA's policy to minimize the regulatory burden on the public which might arise from conflicting requirements which could be promulgated under different regulatory authorities. In keeping with this policy, the final 1983 TSCA GLP Standards, 40 CFR Part 792, followed the format and, with few exceptions, the wording of FDA's final GLP regulations, 21 CFR Part 58. Differences between the EPA and FDA GLP regulations were based upon varying needs and responsibilities under each Agency's regulatory statutes. This proposed revision to the TSCA GLP standards follows this same policy by conforming to many of the changes FDA made to its GLP regulations, published in the **Federal Register** of September 4, 1987 (52 FR 33768). EPA has varied from FDA's revised GLP regulations only when necessary due to EPA's statutory responsibilities. The most significant differences between the EPA proposal and the revised FDA GLP regulations are the scope of the testing and test systems affected.

As in the current TSCA Good Laboratory Practice Standards, the proposed revisions to the TSCA GLP standards vary from the FDA GLPs in that the TSCA GLPs incorporate GLP provisions for environmental testing (EPA is proposing that the FIFRA GLPs extend to environmental studies as well). Environmental studies include ecological effects and chemical fate studies. Ecological effects studies are those performed for development of information on nonhuman toxicity and potential ecological impact of chemicals and their degradation products. Chemical fate studies are studies performed to characterize physical, chemical, and persistence properties of a substance in order to evaluate the transport and transformation of the substance in the environment.

To ensure the quality and integrity of all data generated from environmental studies, the current TSCA GLP standards contain requirements within 40 CFR Part 792 Subpart L applicable to testing plants, microbial organisms, aquatic organisms, amphibians, reptiles, and birds, where appropriate. These requirements include provisions for care, care facilities, and supply facilities for the various test systems used in environmental testing. As a means of simplifying the regulations, EPA is proposing that the requirements currently found within Subpart L be merged into Subparts A through J of the TSCA GLPs. Accordingly, it is proposed that current § 792.43 *Animal care facilities,* § 792.45 *Animal supply facilities,* and § 792.90 *Animal care* incorporate the provisions relating to the care of test systems, care facilities, and supply facilities from § 792.228 in Subpart L. The expanded sections are retitled in the proposed revision as follows: § 792.43 *Test system care facilities,* § 792.45 *Test system supply facilities,* and § 792.90 *Animal and other test system care.* Further, in most instances, EPA is proposing to replace the term "animal," currently used in the EPA and FDA GLP regulations, with the broader term "test system." Specifically, this change is proposed in §§ 792.43, 792.45, 792.81, 792.90, and 792.120. These proposed changes are further discussed in Unit I.D. of this preamble.

EPA's proposed TSCA GLP standards also vary from FDA's in their coverage of testing conducted in the field. To ensure the quality and integrity of data submitted to the Agency, EPA believes that GLP standards must apply whenever data collection occurs. Because many of the test data required by EPA are developed in the field, or more accurately in outdoor laboratories (i.e., ground water studies, air monitoring studies, degradation in soil, etc.), EPA is proposing to include field testing within the scope of these regulations.

The remaining differences between the EPA and FDA GLPs are described in the preamble to this proposed rule and the preamble to the TSCA Good Laboratory Practice Standards, published in the **Federal Register** of November 29, 1983 (48 FR 53922). EPA has coordinated this proposal with FDA and has considered comments received on the proposal to amend the FDA GLP regulations (October 29, 1984; 49 FR 43530).

D. Proposed Changes to the TSCA GLP Regulations

1. *Section 792.1 Scope.* EPA proposes to amend § 792.1 to reflect the Agency's option of entering into testing consent agreements in lieu of a test rule under section 4 of TSCA. Consistently, the term "testing consent agreement" has been added to the definition of "test substance" in proposed § 792.3, and has been added in proposed §§ 792.12 and 792.17.

2. *Section 792.3 Definitions.* a. EPA proposes that the definition of the term "carrier" be moved from § 792.226(b) to § 792.3. As stated in Unit I.C. of this

preamble, EPA is proposing to delete Subpart L and include all the provisions of Subpart L within Subparts A through J of the TSCA GLP standards. Therefore, EPA proposes to define the term "carrier" in § 792.3 to mean any material, such as feed, water, soil, nutrient material, etc., with which the test substance is combined for administration to test organisms.

b. EPA proposes to conform with the September 4, 1987, FDA GLP regulations by amending the definition of "control substance" to exclude feed and water. EPA agrees with FDA's statement regarding this change (52 FR 33769: September 4, 1987) that "the term control [substance] should be reserved for the discrete substances/articles, and vehicles other than feed and water administered to groups of the test system to provide a basis of comparison with the test [substance]."

FDA contends that, under the current definition of "control substance," because the control group of a test system provides the basis for comparison with a test substance, any substance administered to the control group is considered a control substance. This means that feed and water given to the control group of a study are considered a control substance. For instance, in studies in which the test substance or mixture is administered to the test system orally, through feed or drinking water, gavage, or injection, the feed or water is considered a control substance. As a control substance, the feed or water is subject to § 792.105(a) for substance characterization, § 792.105(b) for testing for stability and solubility, § 792.105(c) for requirements for appropriate storage, § 792.105(d) for retention of reserve samples, and § 792.107 for documentation of receipt and distribution of each batch. EPA agrees with FDA that placing these requirements on the use of feed and water as a control substance in control groups unnecessarily burdens the regulated community and is not essential for ensuring the quality and integrity of the data generated by a study.

However, under 40 CFR Part 792, feed and water used as a carrier for the test and control substances or mixtures are still covered by the applicable sections for the testing and storage of test, control, and reference substances and mixtures. For example, § 792.31(e) requires testing facility management to ensure that materials are available as scheduled; § 792.45 requires that test system supply facilities shall be provided to ensure proper feed storage; § 792.81(b)(2) requires Standard Operating Procedures (SOP) for test system care, including nutrition; § 792.90(g) requires periodic analysis of feed and water to ensure that contaminants which would interfere with the study are not present; § 792.120(a)(9) requires the protocol to describe and/or identify the diet used in the study, including the level of contaminants expected in the dietary materials.

c. EPA also proposes to modify the definition of "control substance" by adding the phrase "for no effect levels." This addition to the definition is being proposed merely to clarify the difference between the term "reference substance" and "control substance." While a control substance is used to determine a baseline comparison for no effect levels, a reference substance is used to determine a baseline comparison to an established effect level.

d. EPA proposes to add and define the terms "experimental start date" and "experimental termination date." "Experimental start date" is proposed to mean the first date the test substance is applied to the test system. Under this definition, as of the experimental start date: (1) Under proposed § 792.105(b), the stability and, if important to the conduct of the experiment, the solubility of the test, control, and reference substance would have to be determined; (2) under proposed § 792.113(a)(2), the stability and, when important to the conduct of the experiment, the solubility of the test, control, and reference substance in the mixture would have to be determined and; (3) under proposed § 792.120(a)(4), the proposed experimental start date would appear in the protocol.

EPA proposes that "experimental termination date" be defined as the last date on which data are collected directly from the study. Under § 792.120(a)(4), as proposed, EPA would require the proposed experimental termination date to appear in the protocol. EPA considers histopathology after scheduled terminal animal sacrifice to be carried out before the experimental termination date.

Experimental start and termination dates would be expressed as the actual calendar dates, not just time-line increments. Therefore, when determining the proposed experimental start and termination dates, as would be required by proposed § 792.120(a)(4), the submitter should consider any lag time relating to protocol approval and laboratory contracting.

e. EPA proposes to add and define the term "reference substance". This term is currently defined in § 792.226(f) to mean any chemical substance or mixture or material other than a test substance that is administered to or used in analyzing the test system in the course of a study for purposes of establishing a basis for comparison with the test substance. EPA proposes to add the phrase "for known effect levels" to this definition to more clearly distinguish the terms "reference substance" and "control substance" (see discussion of the term "control substance" in Unit I.D. of this preamble).

Consistent with the Agency's proposal to merge the provisions of Subpart L into Subparts A through J, all the requirements provided for test and control substances are being proposed to apply to "reference substances." Accordingly, the term "reference substance" has been added wherever the term "test and control substance" appears in these regulations. Specifically, it is proposed that the term "reference substance" be added to § 792.29 (d) through (f); § 792.43(b); § 792.47(a) (1) through (3) and (b); § 792.61(b)(3); § 792.90(e); the Subpart F heading; § 792.105 (a) through (e); § 792.107; § 792.113 (a) and (b); § 792.120(a) (2), (9), and (11); § 792.185(a) (4) and (5); and § 792.195(c).

f. EPA proposes to amend the definition of "sponsor" by replacing the term "negotiated testing agreement" with the term "testing consent agreement." This proposal reflects the Agency's option of entering into a section 4 testing consent agreement in lieu of a test rule promulgated under section 4 of TSCA.

g. EPA proposes to broaden the definition of the term "study" to be consistent with the scope of testing that may be submitted under TSCA sections 4 and 5.

EPA is proposing to delete the phrase "in vivo or in vitro" from the definition of "study." The Agency still intends the requirements of these regulations to apply to "in vivo and in vitro" experiments. However, since the Agency intends these regulations to apply to all studies required to be developed under TSCA, including those conducted in the field, EPA believes that the phrase "in vivo or in vitro" in the current definition of "study" is too limiting.

Further, EPA is proposing to delete the term "prospectively" from the definition of "study." In this way, epidemiological studies, which could be "retrospective," will be required to be presented to the Agency in accordance with the GLP standards. EPA recognizes that data used in an epidemiological study may not have been generated in conformance

with the TSCA GLP standards, however, it is EPA's contention that the epidemiological study itself can be conducted and submitted to the Agency in accordance with the GLPs.

EPA is also proposing to delete from the current definition of "study" the following sentence: "The term does not include studies utilizing human subjects or clinical studies or field trials in animals." Again, this change is consistent with EPA's intention that all studies follow GLPs which are required to be conducted under TSCA.

h. EPA proposes to incorporate the FDA definitions for "study completion date" and "study initiation date" into the TSCA GLP standards in § 792.3. "Study completion date" is proposed to mean the date the final report is signed by the study director. EPA advises that the phrase "close of the study" as used in § 792.33(f) refers to the "study completion date." Therefore, as of that date: (1) Under § 792.33(f), the study director must ensure that all raw data, documentation, protocols, specimens, and final reports are transferred to the archives; and (2) after this date under § 792.185(c), corrections or additions to the final report must be in the form of an amendment by the study director under the procedures specified in that section.

EPA proposes to define "study initiation date" as the date the protocol is signed by the study director. EPA advises that the phrase "study is initiated" as used in § 792.31(a), and the phrase "study was initiated" as used in § 792.35(b)(1) refer to the "study initiation date." Therefore, as of the study initiation date: (1) Under § 792.31(a), the testing facility management would designate a study director; (2) under § 792.35(b)(1), the study would be entered on the master schedule sheet by the quality assurance unit; and (3) under § 792.120(b), after this date all changes or revisions in the protocol would be documented, signed by the study director, and dated. EPA also expects that as of the study initiation date, under § 792.31(e), the testing facility management would have ensured that personnel resources, facilities, equipment, material, and methodologies are available as scheduled.

i. EPA proposes to replace the term "test substance or mixture" with the term "test substance." This is an editorial change which makes usage consistent in the GLP standards. The term "test substance" is proposed to be defined to include mixtures.

j. EPA proposes to incorporate the definition of the term "test system" currently found at § 792.226(a) into the definition of "test system" currently found at § 792.3(p). Therefore, the proposed definition of "test system" in proposed § 792.3 will include chemical or physical matrices (e.g., soil or water).

k. EPA proposes to incorporate the term "vehicle" currently found in § 792.226(g) into § 792.3 *Definitions.*

3. *Section 792.31 Testing facility management.* In conformance with the revised FDA GLP regulations, in § 792.31(b), EPA proposes to delete the requirement that the replacement of a study director must be documented as "raw data." EPA agrees with FDA that this requirement is redundant with other provisions of the GLPs. For instance, § 792.35(b)(1) states that the master schedule sheet must contain the name of the study director. As FDA notes (52 FR 33770), any replacement of the study director would be reflected on the master schedule sheet, which is already considered "raw data." Further, § 792.120(b) states that all changes in an approved protocol must be documented and signed by the study director. Replacement of the study director is considered to be a change in the approved protocol.

4. *Section 792.35 Quality assurance unit (QAU).* a. In § 792.35(a), EPA proposes to conform with the revised FDA GLP regulations by substituting the term "which" for the current phrase "composed of one or more individuals who." This change clarifies that EPA does not require the QAU to be a fixed, permanently staffed unit whose only functions are to monitor the quality of a study. The Agency is only concerned that there be a distinct separation of duties between those personnel involved with the conduct or direction of a study and those personnel performing quality assurance on the same study. Therefore, EPA does intend proposed § 792.35(a) to prohibit personnel from performing quality assurance activities on their own study.

b. In § 792.35(b)(1), EPA proposes to delete the requirement that the name of the study sponsor appear on the master schedule sheet. Instead, it is proposed that under § 792.35(b)(1) the sponsor's identity appear on the master schedule sheet. This change is being proposed to be consistent with the FDA's recent revision and to provide the regulated community the option of using an identity code on the master schedule in lieu of the sponsor's name.

EPA agrees with FDA's contention that requiring the sponsor to be identified specifically by name on the master schedule is not essential to fulfill the requirements of the GLPs or the goal of ensuring the quality and integrity of the data generated from the studies. However, while the name of the study sponsor would not be required to appear on the master schedule sheet, this information must be made available to the Agency upon request.

c. As in the revised FDA GLP regulations, EPA is also proposing to delete the requirement in § 792.35(b)(1) that the master schedule sheet contain the status of the final report. EPA agrees with FDA that this requirement is redundant in view of the other information required by § 792.35(b)(1) such as the date the experiment began and the current status of each study.

d. In conformance with the revised FDA GLP regulations, EPA proposes to modify the requirements of § 792.35(b)(3) to provide for inspections of a study on a schedule adequate to ensure the integrity of the study. This section currently specifies that the quality assurance unit must inspect each phase of a study periodically. This section also currently specifies that for studies lasting more than 6 months, quality assurance inspections shall be conducted every 3 months, and for studies lasting less than 6 months, quality assurance inspections shall be conducted at intervals adequate to ensure the integrity of the study.

The proposed changes to this section will allow the QAU the necessary latitude to adjust its monitoring activities to meet the individual problems of each study. EPA agrees with FDA's contention that an inspection of each phase of the study is not necessary to ensure that a study is being conducted properly. However, EPA also agrees with FDA that each study, no matter how short, must be inspected at least once while in process. EPA expects that by allowing the QAU flexibility in designing a reasonable inspection schedule, the goal of ensuring the quality of the study can be best achieved.

e. Consistent with the revised FDA GLPs, EPA is proposing to delete § 792.35(e) in its entirety. Section 792.35(e) currently requires that all quality assurance records be kept in one location at the testing facility. As FDA pointed out in its October 29, 1984, proposed GLP revision, since § 792.190(b) already requires the use of archives for the orderly storage and expedient retrieval of all reports and records, the requirements of § 792.35(e) are not necessary. However, EPA maintains that all reports and records, including those of the QAU, must be easily accessible and made available to EPA and FDA inspectors when requested.

5. *Section 792.41 General.* FDA has deleted from its GLPs the requirement

that the location of each testing facility be suitable to facilitate the proper conduct of studies. However, EPA is proposing that § 792.41 require that testing facilities which are not located within an indoor controlled environment be suitably located to facilitate the proper conduct of studies.

The studies FDA requires are generally conducted within the confines of a traditional indoor laboratory. Because the conditions specified within a protocol can be artificially manipulated within the traditional indoor laboratory, the location of these laboratories is generally not a factor in determining the quality of a study. Therefore, it is not necessary to ensure that a traditional indoor testing facility is suitably located to facilitate the proper conduct of the study.

However, the studies EPA requires are not necessarily conducted within the confines of the traditional indoor scientific laboratory (i.e., field studies, exposure monitoring studies, ecological toxicity studies, etc.). EPA considers any site where testing is undertaken to generate data required by the Agency to be a testing facility. The conditions required by the protocol are not necessarily conducive to artificial manipulation in the field, or other outdoor testing facilities. Therefore, ensuring the suitability of the location of these types of testing facilities is both a valid and necessary part of EPA's GLP Standards.

6. *Section 792.43 Test system care facilities.* a. EPA is proposing to revise the title of § 792.43 from "Animal care facilities" to "Test system care facilities." The proposed heading for § 792.43 more adequately reflects the Agency's intent to specify within the main body of the TSCA GLP Standards the requirements for testing facilities for the care of chemical or physical matrices (e.g., soil or water), plants, and microorganisms, as well as animals. Accordingly, the Agency is proposing to further modify § 792.43 by incorporating the term "test system" when facility requirements should extend beyond "animal" care.

b. Consistent with the Agency's intent to incorporate the environmental testing provisions currently found in Subpart L into Subparts A through J of Part 792, paragraphs (a)(1), (a)(2), (d), (e), (f), (g), and (h) in proposed § 792.43 have been added or modified to incorporate the provisions currently found in § 792.228(b) (1) through (7).

c. EPA proposes to modify § 792.43(a) to allow esting facilities to provide for isolation areas rather than quarantine areas. This change is consistent with the proposal to modify § 792.90(b) to allow "isolation" of newly received animals rather than requiring "quarantine" [See Unit I.D. of this preamble for. a discussion of proposed § 792.90(b)].

d. In § 792.43(c), EPA proposes to delete the requirement that separate areas be provided in all cases for the diagnosis, treatment, and control of test system diseases. Instead, it is proposed that such separate areas be provided "as appropriate." This proposal is consistent with the September 4, 1987, revised FDA GLP regulations.

EPA has proposed this modification in order to allow laboratories the option of disposing of diseased animals and other test systems from the experiment without also bearing the expense of maintaining separate areas in testing facilities for diagnosis, treatment, and control of disease. Additionally, EPA recognizes that the diagnosis and treatment requirements of § 792.43(c) may not be appropriate when dealing with such test systems as soil, plants, or microorganisms. However, if the decision is made not to dispose of the test system from the study, then test system care facilities, as specified in proposed § 792.43(c), must be provided.

e. EPA proposes to conform to the revised FDA GLPs by deleting § 792.43(e) in its entirety. Currently, § 792.43(e) requires test system facilities to be designed, constructed, and located so as to minimize disturbances which may interfere with the study. EPA agrees with FDA that this provision is already adequately covered in § 792.41, which requires that facilities be of suitable size construction, and, for outdoor testing facilities, location to facilitate the proper conduct of the study.

7. *Section 792.45 Test system supply facilities.* a. EPA proposes to incorporate the provisions of § 792.228(c) into § 792.45. Therefore, proposed § 792.45 will require that supply facilities necessary for environmental testing be provided when appropriate.

b. Consistent with the proposed expanded scope of this section, EPA is also proposing to retitle § 792.45 from "Animal supply facilities" to "Test system supply facilities."

c. EPA proposes to modify § 792.45 to state "Perishable supplies shall be preserved by appropriate means." This change is being proposed to conform with the revised FDA GLPs and recognizes that there are a variety of acceptable storage and preservation procedures available other than refrigeration. Depending on the stability characteristics of the perishable material, acceptable storage and preservation methods may include desiccation, room temperature-low humidity, and constant temperature-low humidity.

d. EPA also proposes to delete the phrase "or feed" from the last sentence of § 792.45. Both EPA and FDA consider "feed" to be a "supply." Therefore, the use of the word "feed" in § 792.45 is redundant.

8. *Section 792.49 Laboratory operation areas.* a. EPA proposes to conform with FDA's revised GLP regulations by deleting paragraph (b) from § 792.49, adding the phrase "and specialized" after the word "routine" and before the word "procedures," and deleting the qualifying phrase "including specialized areas for performing activities such as aseptic surgery, intensive care, necropsy, histology, radiography, and handling of biohazardous materials."

Paragraphs (a) and (b), as currently worded, describe activities which require that separate laboratory space be provided. As FDA noted in its proposal to modify its corresponding section, the list of activities that currently appears in paragraphs (a) and (b) is not all inclusive and is not essential for the clarity of these sections. Further, by adding the phrase "and specialized," the proposed new paragraph will encompass all activities now listed in paragraphs (a) and (b).

b. In § 792.49, EPA proposes to add the phrase "and other space" after the words "laboratory space" and before the word "shall." As discussed in Unit I.C. of this preamble, this change to § 792.49 is being proposed to reflect that testing does not necessarily take place within the confines of a traditional indoor laboratory. Proposed § 792.49 would require that there be enough space provided to perform the procedures required by the protocol wherever testing takes place (i.e., indoor laboratory or field station).

9. *Section 792.53 Administrative and personnel facilities.* As in the revised FDA GLP regulations, EPA proposes to delete § 792.53 in its entirety. EPA agrees with FDA that the requirements of this section are not necessary for achieving the goals of the TSCA GLP standards.

10. *Section 792.61 Equipment design.* In § 792.61, EPA proposes to delete the phrase "Automatic, mechanical, or electronic" from the beginning of the first sentence. EPA agrees with FDA that the deletion of these qualifying terms provides for a more general interpretation of the word "equipment."

11. *Section 792.63 Maintenance and calibration of equipment.* a. Consistent with the FDA GLPs, EPA is proposing to amend § 792.63(b) to state that standard

operating procedures (SOPs) for remedial action for equipment, in the event of failure or malfunction of equipment, need only be established when "appropriate." This change acknowledges that laboratories may choose to discard rather than repair equipment, and in such cases SOPs which delineate remedial action are not necessary.

b. EPA is also proposing to conform to the revised FDA GLP regulations by deleting from § 792.63(b) the provision that copies of the SOPs shall be made available to laboratory personnel. EPA still believes that laboratory personnel must have access to laboratory SOPs; however, since this requirement is clearly stated in § 792.81(c), EPA considers the inclusion of this provision in § 792.63(b) to be redundant.

12. *Section 792.81 Standard operating procedures.* a. In § 792.81(b) (1), (2), (6), (7), and (12), EPA is proposing to replace the term "animal" with the term "test system." As discussed previously in this preamble, this modification is consistent with the broad scope of test systems which may be used in environmental testing. Further, the Agency proposes to extend all the SOP requirements outlined by § 792.81 to environmental testing. For instance, the provisions of proposed § 792.81(b)(11), which require SOPs for the maintenance and calibration of equipment, would apply to procedures for preparation and maintenance of incubators, greenhouses, or growth chambers, currently required under § 792.228(d).

b. In § 792.81(b)(5), EPA is proposing to require that SOPs be established for tests wherever the testing is undertaken, including those conducted in the field. Accordingly, it is proposed that § 792.81(b)(5) read "Laboratory or other tests" (see discussion of "field testing" in Unit I.C. of this preamble).

c. In conformance with FDA's revised GLP regulations, EPA is proposing to delete the list of examples for laboratory manuals and SOPs required to be made immediately available under § 792.81(c). EPA still intends that laboratory areas must have immediately available manuals and SOPs for laboratory procedures being performed. This requirement still includes toxicology, histology, clinical chemistry, hematology, teratology, and necropsy, if applicable. However, this list is not all inclusive and is too broad to serve as a useful guide. For example, this requirement also includes SOPs for the maintenance, repair, and calibration of equipment as described in § 792.63(b).

d. EPA is also proposing to amend the language of § 792.81(c) to clarify that the requirement of this section also applies to field testing facilities. Therefore, it is proposed that § 792.81(c) will read, "Each laboratory *or other study* area shall have immediately available manuals and standard operating procedures relative to the laboratory or field procedures being performed."

13. *Section 792.90 Animal and other test system care.* a. EPA is proposing to retitle § 792.90 from "Animal care" to "Animal and other test system care." As previously stated, testing required by EPA may involve plants, soils, microorganisms, and other test systems, in addition to animals. The proposed title to § 792.90 reflects the broader scope of test systems for which the EPA intends this section to apply.

Further, it is proposed that the provisions for test system care for ecological effects testing, found in § 792.228(e), be incorporated into proposed § 792.90. Specifically, the proposed revision incorporates the requirements of: § 792.228(e)(1) into proposed § 792.90(b), § 792.228(e)(2) into proposed § 792.90(d), § 792.228(e)(3) into proposed § 792.90(e)(1), § 792.228(e)(4) into proposed § 792.90(f), § 792.228(e)(5) into proposed § 792.90(g), and § 792.228(e)(6) into proposed § 792.90(j).

b. EPA proposes to modify § 792.90(b) to provide for the evaluation of a test system's health status, or the appropriateness of the test system for the study, according to acceptable "scientific practice." This section, as proposed, will still require that newly received animals must have their health status evaluated according to acceptable veterinary medical practices. However, EPA recognizes that it may not be appropriate to evaluate the health status of certain test systems (e.g., soil or water) or to require that a plant, microorganism, soil, or water be evaluated according to acceptable veterinary medical practice to determine their appropriateness for a study. EPA is only concerned that test systems used in a study are free of any disease or condition which may interfere with the purpose or conduct of the study, and that the proper precautions, as stated in § 792.90(b), are taken to comply with this requirement.

c. Additionally, EPA is proposing to modify § 792.90(b), to require "isolation" rather than "quarantine" of newly received animals. This proposal is consistent with FDA's revision to its GLP regulations.

As previously stated, the intent of § 792.90(b) is to prevent the entry of unhealthy or inappropriate test systems into the study, as required by § 792.90(c). Currently, § 792.90(b) provides that this intent be achieved through "quarantine." However, the term "quarantine" suggests a rigid set of procedures, including a mandatory holding period, a specific list of diagnostic procedures, and the use of specialized facilities and test system care practices, which may be an unnecessary burden to industry.

EPA agrees with FDA's conclusion, discussed in the preamble to its revised GLP regulation (52 FR 33775; September 4, 1987), that isolation and evaluation of health status are sufficient precautions against contamination of test systems and, therefore, fulfill the intent of this section. FDA further states that such a revision would provide laboratories the flexibility to develop isolation and health status evaluation procedures best suited for the age, species, class, and type of the test system, as well as the type of study to be performed.

d. EPA proposes to conform to the FDA GLPs by modifying § 792.90(c) to require isolation of diseased test systems only when necessary.

Currently, § 792.90(c) requires that animals which contract a disease or condition shall be isolated in all cases. This requirement would in turn require that separate facilities be available for the isolation of these animals. However, as discussed in the proposal for § 792.43(c), both EPA and FDA believe that laboratories should be given flexibility in their disposition of diseased test systems. As FDA discussed in the proposed revisions to its GLP regulations (49 FR 43533; October 29, 1984), the proposed modification to § 792.90(c) will allow laboratories the option of: (1) Leaving the diseased test system in the experiment provided that the integrity of the study will not be adversely affected by this action; (2) disposing of the test system; or (3) isolating, treating, and returning the test system to the study.

14. *Section 792.105 Test, control, and reference substance characterization.* a. In revised 21 CFR 58.105(a), FDA has deleted the requirement that test and control substance characteristics shall be determined and documented for each batch "before the initiation of the study." This change has not been incorporated by EPA in its proposed revision to § 792.105(a). However, EPA proposes to modify § 792.105(a) to require that test, control, *or reference* substance characterization be determined and documented for each batch before its use in the experiment. EPA feels that this proposed requirement is necessary because it is essential that characteristics of test, control, and reference substances be known prior to their administration or use in an experiment.

EPA's recent experience with antimony trioxide has shown that extensive analytical work was necessary prior to test initiation. Certain assumptions regarding the product's characteristics were used in the protocols for antimony trioxide testing which proved invalid. These invalid assumptions necessitated modifications to the proposed study, resulting in the delay and rescheduling of other subsequent studies. If the analytical work had preceded the toxicology studies, the studies would not have failed and modifications to the studies woul d not have been necessary. The Agency's conclusion is that it is better to delay study schedules than to initiate improper experimental procedures which will produce invalid results.

b. FDA has modified 21 CFR 58.105(b) to provide for the determination of the stability of the test or control substance either before the initiation of the study or through periodic analysis of each batch according to written standard operating procedures. EPA has chosen not to adopt this approach in proposed § 792.105(b) because the Agency does not agree that stability can adequately be demonstrated by periodic analysis without initial evaluation.

Further, there are many studies required by EPA where solubility of the test, control, and reference substance is of critical importance, such as aquatic toxicity studies. Therefore, EPA is proposing that solubility of the test, control, and reference substance be determined before the experimental start date if knowledge of the solubility characteristics is relevant for the proper conduct of the experiment.

It is EPA's contention that both stability and solubility of the test, control, and reference substance need to be determined before the experimental start date in order to ensure proper handling and administration of the test substance to the test system. However, since the determination of the solubility of the test, control, and reference substance is not a requirement in FDA's GLP regulations, EPA is interested in receiving public comment on this issue.

15. *Section 792.113 Mixtures of substances with carriers.* a. FDA has modified 21 CFR 58.113(a)(2) to require determination of the stability of the test and control substance in a mixture, as required by the conditions of the study, either before the initiation of the study or through periodic analysis of each batch. While EPA does not propose to modify § 792.113(a)(2) to provide the option of determining the stability of the mixture either before study initiation or through periodic analysis (see discussion for § 792.105(b)), EPA will modify this section to require stability testing only to the extent required by the conditions of the experiment. As proposed for § 792.105(b), EPA is also proposing to require that, when appropriate to the conduct of the experiment, solubility of the test, control, or reference substance in the mixture must be determined in the same manner (see discussion for § 792.105(b)). Additionally, as proposed for § 792.105 (a) and (b), EPA is proposing to replace the phrase "before the initiation of the study" with the phrase "before the experimental start date" (see discussion for § 792.105(a)).

The phrase "as required by the conditions of the experiment" has been added in order to clarify that determination of stability and, if appropriate, solubility of a test, control, or reference substance in a mixture is only necessary to support its actual time of use in the experiment. Therefore, it is not necessary to provide data which illustrate long-term stability of a mixture when the actual time that the mixture is used is short-term. For example, a test, control, or reference substance in a mixture that will be used the same day it is prepared will only require data sufficient to show stability and, if appropriate, solubility for 1 day.

b. Additionally, EPA proposes to incorporate into § 792.113(a)(2), the provision currently found in § 792.228(f)(2), which states that the determination of the stability or solubility of the test, control, or reference substance in the mixture must be done under the environmental conditions specified in the protocol.

c. EPA proposes to add new paragraph (c) to § 792.113 which incorporates the provisions of § 792.228(f)(3).

16. *Section 792.120 Protocol.* a. In 21 CFR 58.120(a), FDA has replaced the qualifying phrase "but shall not necessarily be limited to" with the phrase "as applicable." EPA proposes to adopt FDA's approach with some modifications. It is proposed that the phrase "Where applicable" appear before the information specified in § 792.120(a)(9), and continue to appear before the information required by § 792.120(a)(6). The phrase "but shall not necessarily be limited to" would remain in this section.

In FDA's discussion of this proposal (49 FR 43533; October 29, 1984), concerns were expressed that some of the information required to appear in the protocol is not applicable to all types of testing. Specifically, FDA points to the information required by 21 CFR 58.120(a) (9) and (11). In 21 CFR 58.120, paragraph (a)(9) requires a description of the diet used in a study as well as solvents, emulsifiers, and/or other materials used to solubilize or suspend the test or control substance before mixing with the carrier. FDA points out that this requirement is not applicable to radiation-emitting products. Section 58.120(a)(11) specifies that the protocol shall specify dosage level, and this requirement is not applicable to implantable medical devices.

Clearly, the basis for FDA's change is to accommodate concerns that are specific to the types of testing required by FDA and do not necessarily apply to testing required by EPA. Further, EPA is concerned that placing the phrase "as applicable" in § 792.120(a) suggests that there may be cases where it is not applicable for any of the other information required by § 792.120(a) to appear in the protocol. Therefore, the phrase "as applicable" should only appear before those items which are not necessarily appropriate to appear in the protocol for certain types of testing.

For example, there may be testing required by EPA where it may not be appropriate to require a protocol to contain the information specified in § 792.120(a)(9), such as describing and/or identifying the diet of a human subject involved in exposure testing. Therefore, EPA proposes to add the phrase "Where applicable" before the information specified in proposed § 792.120(a)(9).

b. In 21 CFR 58.120(a)(4), FDA has deleted the requirement that the protocol contain "The proposed starting and completion dates." EPA is proposing to retain this requirement in § 792.120(a)(4), but is proposing to modify this paragraph to require, "The proposed experimental start and termination dates."

EPA believes that this information is necessary for the evaluation of a protocol and the Agency's scheduling of additional related studies and audit reviews. Section 792.120(a)(4) is related to the selected study method, laboratory, and specialist availability, and other Agency and industry priorities. Often a group of experiments are carried out in sequence, so that both start and termination dates affect subsequent study expectations and timetables. Projected experimental start and termination dates identify the normal duration for a given experiment type and reflect any special considerations that may be unique to a laboratory, anticipated analytical or methodology work, and available resources, and it may also affect pending regulatory timetables.

Given that there are hundreds of studies that EPA must track, these estimated schedules, combined with those from other studies, allow the Agency to more efficiently schedule audits and regulatory action. Further considerations are the following: (1) The availability of composite schedules for many studies may be necessary to set realistic regulatory action goals; (2) composite study schedules are evaluated to schedule audits while several studies are ongoing or recently completed, and which may all be at a given laboratory or geographic location. This directly reduces EPA resources necessary for audit and regulatory review functions; and (3) standard business management by objectives requires intermediate calendar goals when scheduling multiple outputs, or a long-term single product. The master on-site laboratory schedule will incorporate these dates to carry out the study.

c. In 21 CFR 58.120(a)(5), FDA has deleted the requirement that the protocol contain a justification for the selection of the test system. EPA has chosen to retain this requirement in proposed § 792.120(a)(5).

Environmental studies, including both ecological effects and chemical fate, are more diverse than health effects testing. Further, details relevant to the test system design are more chemically dependent in the case of environmental effects and chemical fate testing than in the case of health effects testing. Many of the test systems in environmental studies must be modified in accordance with specific chemical characteristics. Therefore, EPA must allow a much broader range of flexibility in the nature of tests and selection of test systems. In order to fully understand the test and its results, EPA needs to have a discussion of the reasons for selection of the test system. In addition, EPA recognizes that industry may be engaged in state-of-the-art environmental testing. Under proposed § 792.120(a)(5), EPA can keep abreast of industry advances in such testing and ensure that their use of test systems is appropriate. EPA is interested in receiving public comment on whether to limit the requirement that the protocol contain a justification of the test system to environmental testing.

d. FDA has deleted from 21 CFR 58.120(a)(10) the requirement that the protocol include the route of administration and the reason for its choice. EPA has chosen to retain this requirement in proposed § 792.120(a)(10).

The chemicals regulated by FDA will usually have a predefined route of exposure. Therefore, it makes sense for FDA to eliminate the requirement to stipulate the route of administration and the reason for its choice within the protocol. Unlike FDA, EPA is concerned with presence in or exposure to various media (i.e., air, water, soil, sediment, chemicals, etc.) and may not know in advance the routes of exposure for the chemicals it regulates. Most chemicals and products regulated by EPA do not have set routes of exposure and may even have multiple routes of exposure. Therefore, EPA must consider a wide range of possible exposure routes in its regulatory decisions. Further, the route of administration is essential to determine the effectiveness of a test system for the purposes of a specific toxicology study. The route of administration affects the real dosage rates, and therefore, affects whether the impact of the exposure of the test substance is acute or chronic.

Therefore, EPA believes that, for its purposes, it is essential that the protocol contain the route of administration and the reason for its choice. This requirement will therefore remain in the EPA's TSCA GLP standards in § 792.120(a)(10).

e. EPA proposes to delete current § 792.120(a)(12) in its entirety. Currently, § 792.120(a)(12) requires that the protocol contain the method by which the degree of absorption of the test and control substance by the test system will be determined. EPA agrees with FDA's conclusion that this requirement is not necessary in the protocol.

f. In proposed § 792.120(a)(14), redesignated from current paragraph (a)(15), EPA proposes to conform with FDA's revised GLP regulations and require that the study director's signature be dated on the protocol.

EPA is proposing in § 792.3 that the study initiation date be defined as the date the protocol is signed by the study director. It is through the proposed requirement of § 792.120(a)(14), that the Agency will be able to identify the official study initiation date.

17. *Section 792.130 Conduct of a study.* a. FDA has modified 21 CFR 58.130(d) to provide that records of gross findings for a specimen from postmortem observations "should" be made available to the pathologist when examining that specimen's histopathology. EPA has chosen to retain the requirement that these records "shall," in all cases, be provided to a pathologist during study of the specimen.

EPA agrees with FDA's conclusion that for most studies it is important for the pathologist to have the records of gross findings available when examining a specimen histopathologically. However, it is FDA's contention that replacing the word "shall" with the word "should" will allow the histopathological evaluation of specimens in a "blind" fashion. EPA also recognizes that it may be appropriate for some studies to provide for "blinding" in histopathological evaluation. However, EPA maintains that, when specified by the protocol, the pathologist can accomplish "blinding," without violating § 792.130 by not looking at the records which have been provided. Therefore, it will remain EPA's requirement that the pathologist must have access to the records of gross findings when examining a specimen histopathologically.

b. In conformance with the revised FDA GLP regulations, in § 792.130(e), EPA proposes to replace the terms "computer" and "computer driven" with the term "automated data collection." EPA agrees with FDA that the terms "computer" or "computer driven" do not adequately reflect the data collection and storage technologies currently used by testing facilities. The Agency believes that the proposed term "automated data collection" provides a more appropriate description of the data collection and storage systems available for industry use.

18. *Section 792.135 Physical and chemical characterization studies.* EPA proposes to add § 792.135 in order to specify the provisions of the proposed TSCA GLP standards which will not apply to studies designed to determine the physical and chemical characteristics of a test, control, or reference substance. Most studies designed to determine the physical or chemical characteristics of a test, control, or reference substance rarely involve any modifications to the protocol or experimental design and are usually conducted in an assembly line fashion. Therefore, proposed § 792.135(a) relaxes the requirements of the GLP standards without compromising the quality or integrity of data generated from these studies.

However, in § 792.135(b), EPA is also proposing that the exemptions listed in proposed § 792.135(a) will not apply to studies designed to determine solubility, octanol water partition coefficient, volatility, and persistence of a test, control, or reference substance. These types of physical and chemical characterization studies are more complex in design, execution, and interpretation, and EPA does not believe that it can be assured of the quality and integrity of data generated from these studies without complete GLP compliance.

19. *Section 792.185 Reporting of study results.* In § 792.185(a)(5), EPA is proposing to require that the final report include information relating to the solubility, in addition to stability, of the test, control, or reference substance, if solubility information was important to the conduct of the experiment. This change is consistent with the proposed modifications to §§ 792.105(b) and 792.113(a)(2) (see the preamble discussion of proposed §§ 792.105(b) and 792.113(a)(2)).

20. *Section 792.190 Storage and retrieval of records and data.* a. In § 792.190(a), EPA proposes to conform to the revised FDA GLP regulations by modifying this section to state that specimens obtained from mutagenicity tests and specimens of blood, urine, feces, and biological fluids generated as a result of a study need *not* be retained. EPA is also proposing that § 792.190(a) state that specimens of soil, water, and plants obtained from environmental testing need *not* be retained. EPA agrees with FDA's conclusion that retention of these specimens beyond initial evaluation is burdensome and does not have a significant impact on the quality of a study.

b. As in the revised FDA GLPs, EPA proposes to revise § 792.190(e) by deleting the requirement that study materials which are retained in archives must be indexed specifically by test substance, date of study, test system, and nature of study. EPA agrees with FDA that the intent of this section is to require indexing of materials in such a way as to permit expedient retrieval from archives. EPA does not believe it is necessary to stipulate the specific indexing terms which must be used.

21. *Section 792.195 Retention of records.* a. EPA proposes to delete paragraphs (b)(2) and (3) of § 792.195, redesignate paragraph (b)(1) as (b), and amend paragraph (b) to require a retention period for documentation records, raw data, and specimens of 5 years from the date the results of any study are submitted to the Agency.

Currently, § 792.195(b) requires a retention period for records, raw data, and specimens under paragraph (b)(1) of 10 years following the effective date of the applicable final test rule and, under paragraph (b)(2) of 10 years following the publication date of the acceptance of a negotiated test agreement. This section also recommends a retention period for such materials of 5 years following the date studies are submitted to the Agency under TSCA section 5.

As stated in the preamble to the 1983 TSCA GLP regulation (48 FR 53935; November 29, 1983), EPA believes that it is essential that study records, raw data, and specimens be maintained to provide the Agency with a sufficient period of time to review the study results and implement any appropriate regulatory actions. Further, it is essential that records, raw data, and specimens be available to suppport Agency decisions in case of court challenges to those decisions. However, the Agency sees no reason to vary record retention requirements and has concluded that a record retention period of 5 years from the date the study is submitted to EPA is a sufficient period of time to meet the Agency concerns and goals. Finally, the record retention period proposed in § 792.195(b) is preferable to the timeframes currently required because it is consistent with the requirements currently set forth in the FIFRA GLPs, in 40 CFR 160.195(b)(2), and the FDA Good Laboratory Practice regulations in 21 CFR 58.195(b).

b. In § 792.195, EPA proposes to delete the examples provided in the first sentence of paragraph (c). EPA has proposed this change in conformity with FDA's recent revision because EPA agrees with FDA that these examples do not clarify which materials must be retained from a study and, therefore, are not necessary in this section.

c. EPA is also proposing to modify § 792.195(c) to state that specimens obtained from mutagenicity tests, specimens of soil, water, and plants, and wet specimens of blood, urine, feces, biological fluids, do not need to be retained beyond quality assurance review. This change has been adopted in order to be consistent with the change discussed in proposed § 792.190(a).

d. In new § 792.195(i), EPA proposes to allow records and other "raw data" required by these regulations to be retained either as original records or as true copies, such as photocopies, microfiche, or other accurate reproductions of the original records. This provision would be incorporated in the TSCA GLPs in § 792.195(i) in order to be consistent with the changes to FDA's Good Laboratory Practice regulations.

II. Economic Analysis

The proposal to expand coverage of the TSCA GLP standards to testing conducted in the field is not expected to increase testing costs significantly. Further, the revisions to the TSCA GLP standards which reflect the FDA GLP revisions primarily provide relief from the original GLP standards (ICF 1987). Therefore, these amendments to the TSCA GLPs are not expected to have a significant economic impact on testing under TSCA.

III. Other Regulatory Requirements

A. Executive Order 12291

Under Executive Order 12291, EPA is required to judge whether a rule is a "major" one and is therefore subject to the requirement of a Regulatory Impact Analysis. The proposed amendments of the TSCA Good Laboratory Practice Standards would not be a major rule because they do not meet any of the criteria set forth and defined in section 1(b) of the Order.

B. Regulatory Flexibility Act

The proposed amendments to the TSCA GLP standards are not expected to have a significant impact on a substantial number of small businesses since little or no economic impact is expected from the revision overall.

C. Paperwork Reduction Act

The Office of Management and Budget (OMB) has approved the information collection requirements contained in this proposed rule under the provisions of the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 *et seq.* and has assigned OMB control number 2070–0033. Comments on these requirements should be submitted to the Office of Information and Regulatory Affairs of OMB, marked "Attention: Desk Officer for EPA." The final rule will respond to any OMB or public comments on the information collection requirements.

List of Subjects in 40 CFR Part 792

Good laboratory practices, Laboratories, Environmental protection, Hazardous materials, Chemicals, Recordkeeping and reporting requirements.

Dated: December 8, 1987.

Lee M. Thomas,

Administrator.

Therefore, it is proposed that 40 CFR Part 792 be amended as follows:

PART 792—[AMENDED]

1. The authority citation for Part 792 is revised to read as follows:

Authority: 15 U.S.C. 2603.

2. In § 792.1, by revising paragraphs (a) and (c) to read as follows:

§ 792.1 Scope.

(a) This part prescribes good laboratory practices for conducting studies relating to health effects, environmental effects, and chemical fate testing. This part is intended to ensure the quality and integrity of data submitted pursuant to testing consent agreements and test rules issued under section 4 of the Toxic Substances

Control Act (TSCA) (Pub. L. 94–469, 90 Stat. 2006, 15 U.S.C. 2603 et seq.).

* * * * *

(c) It is the Agency's policy that all data developed under section 5 of TSCA be in accordance with provisions of this part. If data are not developed in accordance with the provisions of this part, the Agency will consider such data insufficient to evaluate the health and environmental effects of the chemical substances unless the submitter provides additional information demonstrating that the data are reliable and adequate.

3. In § 792.3, by removing the alphabetical paragraph designations in paragraphs (a) through (q); by revising the definitions for "Control substance", "Study," and "Test system"; by replacing the term "Test substance or mixture" with "Test substance"; by amending the definition for "Sponsor" by revising paragraph (2) thereunder; and by adding and alphabetically inserting definitions for "Carrier", "Experimental start date", "Experimental termination date", "Reference substance", "Study completion date", "Study initiation date", and "Vehicle", to read as follows:

§ 792.3 Definitions.

* * * * *

"Carrier" means any material (e.g., feed, water, soil, nutrient media) with which the test substance is combined for administration to test organisms.

"Control substance" means any chemical substance or mixture or any other material other than a test substance, feed, or water that is administered to the test system in the course of study for the purpose of establishing a basis for comparison with the test substance for no effect levels.

* * * * *

"Experimental start date" means the first date the test substance is applied to the test system.

"Experimental termination date" means the last date on which data are collected directly from the study.

* * * * *

"Reference substance" means any chemical substance or mixture or material other than a test substance, feed, or water that is administered to or used in analyzing the test system in the course of a study for purposes of establishing a basis for comparison with the test substance for known effect levels.

* * * * *

"Sponsor" means:

* * * * *

(2) A person who submits a study to the EPA in response to a TSCA section 4(a) test rule and/or a person who submits a study under a TSCA section 4 testing consent agreement or a TSCA section 5 rule or order to the extent the agreement, rule or order references this part; or

* * * * *

"Study" means any experiment in which a test substance is studied in a test system under laboratory conditions or in the environment to determine or help predict its effects, metabolism, environmental and chemical fate, persistence, or other characteristics in humans, other living organisms, or media. The term does not include basic exploratory studies carried out to determine whether a test substance has any potential utility.

"Study completion date" means the date the final report is signed by the study director.

* * * * *

"Study initiation date" means the date the protocol is signed by the study director.

* * * * *

"Test substance" means a substance or mixture administered or added to a test system in a study, which substance or mixture is used to develop data to meet the requirements of a TSCA section 4(a) test rule and/or is developed under a TSCA section 4 testing consent agreement or section 5 rule or order to the extent the agreement, rule or order references this part.

"Test system" means any animal, plant, microorganism, chemical or physical matrix (e.g., soil or water), or subparts thereof, to which the test, control, or reference substance is administered or added for study. "Test system" also includes appropriate groups or components of the system not treated with the test, control, or reference substance.

* * * * *

"Vehicle" means any agent which facilitates the mixture, dispersion, or solubilization of a test substance with a carrier.

4. In § 792.12, by revising the introductory text to read as follows:

§ 792.12 Statement of compliance or non-compliance.

Any person who submits to EPA a test required by a testing consent agreement or a test rule issued under section 4 of TSCA shall include in the submission a true and correct statement, signed by the sponsor and the study director, of one of the following types:

* * * * *

5. In § 792.17, by revising the introductory text of paragraph (a) and paragraph (c) to read as follows:

§ 792.17 Effects of non-compliance.

(a) The sponsor or any other person who is conducting or has conducted a test to fulfill the requirements of a testing consent agreement or a test rule issued under section 4 of TSCA will be in violation of section 15 of TSCA if:

* * * * *

(c) If data submitted to fulfill a requirement of a testing consent agreement or a test rule issued under section 4 of TSCA are not developed in accordance with this part, EPA may determine that the sponsor has not fulfilled its obligations under section 4 of TSCA and may require the sponsor to develop data in accordance with the requirements of this part in order to satisfy such obligations.

6. In § 792.29, by revising paragraphs (d), (e), and (f) to read as follows:

§ 792.29 Personnel.

* * * * *

(d) Personnel shall take necessary personal sanitation and health precautions designed to avoid contamination of test, control, and reference substances and test systems.

(e) Personnel engaged in a study shall wear clothing appropriate for the duties they perform. Such clothing shall be changed as often as necessary to prevent microbiological, radiological, or chemical contamination of test systems and test, control, and reference substances.

(f) Any individual found at any time to have an illness that may adversely affect the quality and integrity of the study shall be excluded from direct contact with test systems, test, control, and reference substances and any other operation or function that may adversely affect the study until the condition is corrected. All personnel shall be instructed to report to their immediate supervisors any health or medical conditions that may reasonably be considered to have an adverse effect on a study.

7. In § 792.31, by revising paragraph (b) to read as follows:

§ 792.31 Testing facility management.

* * * * *

(b) Replace the study director promptly if it becomes necessary to do so during the conduct of a study.

* * * * *

8. In § 792.35, by revising paragraphs (a) and (b) (1) and (3) and removing paragraph (e) to read as follows:

§ 792.35 Quality assurance unit.

(a) A testing facility shall have a quality assurance unit which shall be responsible for monitoring each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with the regulations in this part. For any given study, the quality assurance unit shall be entirely separate from and independent of the personnel engaged in the direction and conduct of that study.

(b) * * *

(1) Maintain a copy of a master schedule sheet of all studies conducted at the testing facility indexed by test substance and containing the test system, nature of study, date study was initiated, current status of each study, identity of the sponsor, and name of the study director.

* * * * *

(3) Inspect each study at intervals adequate to ensure the integrity of the study and maintain written and properly signed records of each periodic inspection showing the date of the inspection, the study inspected, the phase or segment of the study inspected, the person performing the inspection, findings and problems, action recommended and taken to resolve existing problems, and any scheduled date for re-inspection. Any problems which are likely to affect study integrity found during the course of an inspection shall be brought to the attention of the study director and management immediately.

* * * * *

9. By revising § 792.41 to read as follows:

§ 792.41 General.

Each testing facility shall be of suitable size and construction to facilitate the proper conduct of studies. Testing facilities which are not located within an indoor controlled environment shall be of suitable location to facilitate the proper conduct of studies. Testing facilities shall be designed so that there is a degree of separation that will prevent any function or activity from having an adverse effect on the study.

10. By revising § 792.43 to read as follows:

§ 792.43 Test system care facilities.

(a) A testing facility shall have a sufficient number of animal rooms or other test system areas, as needed, to ensure: proper separation of species or test systems, isolation of individual projects, quarantine or isolation of animals or other test systems, and routine or specialized housing of animals or other test systems.

(1) In tests with plants or aquatic animals, proper separation of species can be accomplished within a room or area by housing them separately in different chambers or aquaria. Separation of species is unnecessary where the protocol specifies the simultaneous exposure of two or more species in the same chamber, aquarium, or housing unit.

(2) Aquatic toxicity tests for individual projects shall be isolated to the extent necessary to prevent cross-contamination of different chemicals used in different tests.

(b) A testing facility shall have a number of animal rooms or other test system areas separate from those described in paragraph (a) of this section to ensure isolation of studies being done with test systems or test, control, and reference substances known to be biohazardous, including volatile substances, aerosols, radioactive materials, and infectious agents.

(c) Separate areas shall be provided, as appropriate, for the diagnosis, treatment, and control of laboratory test system diseases. These areas shall provide effective isolation for the housing of test systems either known or suspected of being diseased, or of being carriers of disease, from other test systems.

(d) Facilities shall have proper provisions for collection and disposal of contaminated water, soil, or other spent materials. When animals are housed, facilities shall exist for the collection and disposal of all animal waste and refuse or for safe sanitary storage of waste before removal from the testing facility. Disposal facilities shall be so provided and operated as to minimize vermin infestation, odors, disease hazards, and environmental contamination.

(e) Facilities shall have provisions to regulate environmental conditions (e.g., temperature, humidity, photoperiod) as specified in the protocol.

(f) For marine test organisms, an adequate supply of clean sea water or artificial sea water (prepared from deionized or distilled water and sea salt mixture) shall be available. The ranges of composition shall be as specified in the protocol.

(g) For freshwater organisms, an adequate supply of clean water of the appropriate hardness, pH, and temperature, and free of contaminants capable of interfering with the study shall be available as specified in the protocol.

(h) For plants, an adequate supply of soil of the appropriate composition, as specified in the protocol, shall be available as needed.

11. By revising § 792.45 to read as follows:

§ 792.45 Test system supply facilities.

(a) There shall be storage areas, as needed, for feed, nutrients, soils, bedding, supplies, and equipment. Storage areas for feed, nutrients, soils, and bedding shall be separated from areas housing the test systems and shall be protected against infestation or contamination. Perishable supplies shall be preserved by appropriate means.

(b) When appropriate, plant supply facilities shall be provided. These include:

(1) Facilities, as specified in the protocol, for holding, culturing, and maintaining algae and aquatic plants.

(2) Facilities, as specified in the protocol, for plant growth (e.g., greenhouses, growth chambers, light banks).

(c) When appropriate, facilities for aquatic animal tests shall be provided. These include aquaria, holding tanks, ponds, and ancillary equipment, as specified in the protocol.

12. By revising § 792.47 to read as follows:

§ 792.47 Facilities for handling test, control, and reference substances.

(a) As necessary to prevent contamination or mixups, there shall be separate areas for:

(1) Receipt and storage of the test, control, and reference substances.

(2) Mixing of the test, control, and reference substances with a carrier, e.g., feed.

(3) Storage of the test, control, and reference substance mixtures.

(b) Storage areas for test, control, and/or reference substance and for test, control, and/or reference mixtures shall be separate from areas housing the test systems and shall be adequate to preserve the identity, strength, purity, and stability of the substances and mixtures.

13. By revising § 792.49 to read as follows:

§ 792.49 Laboratory operation areas.

Separate laboratory space and other space shall be provided, as needed, for the performance of the routine and specialized procedures required by studies.

§ 792.53 [Removed]

14. By removing § 792.53 *Administrative and personnel facilities.*

15. By revising § 792.61 to read as follows:

§ 792.61 Equipment design.

Equipment used in the generation, measurement, or assessment of data and equipment used for facility environmental control shall be of appropriate design and adequate capacity to function according to protocol and shall be suitably located for operation, inspection, cleaning, and maintenance.

16. In § 792.63, by revising paragraph (b) to read as follows:

§ 792.63 Maintenance and calibration of equipment.

* * * * *

(b) The written standard operating procedures required under § 792.81(b)(11) shall set forth in sufficient detail the methods, materials, and schedules to be used in the routine inspection, cleaning, maintenance, testing, calibration, and/or standardization of equipment, and shall specify, when appropriate, remedial action to be taken in the event of failure or malfunction of equipment. The written standard operating procedures shall designate the person responsible for the performance of each operation.

* * * *

17. In § 792.81, by revising paragraphs (b) (1), (2), (3), (5), (6), (7), and (12) and (c) to read as follows:

§ 792.81 Standard operating procedures.

* * * * *

(b) * * *

(1) Test system room preparation.

(2) Test system care.

(3) Receipt, identification, storage, handling, mixing, and method of sampling of the test, control, and reference substances.

* * * * *

(5) Laboratory or other tests.

(6) Handling of test systems found moribund or dead during study.

(7) Necropsy of test systems or postmortem examination of test systems.

* * * * *

(12) Transfer, proper placement, and identification of test systems.

(c) Each laboratory or other study area shall have immediately available manuals and standard operating procedures relative to the laboratory or field procedures being performed. Published literature may be used as a supplement to standard operating procedures.

* * * * *

18. By revising § 792.90 to read as follows:

§ 792.90 Animal and other test system care.

(a) There shall be standard operating procedures for the housing, feeding, handling, and care of animals and other test systems.

(b) All newly received test systems from outside sources shall be isolated and their health status or appropriateness for the study evaluated. This evaluation shall be in accordance with acceptable veterinary medical practice or scientific practice.

(c) At the initiation of a study, test systems shall be free of any disease or condition that might interfere with the purpose or conduct of the study. If during the course of the study, the test systems contract such a disease or condition, the diseased test systems should be isolated, if necessary. These test systems may be treated for disease or signs of disease provided that such treatment does not interfere with the study. The diagnosis, authorization of treatment, description of treatment, and each date of treatment shall be documented and shall be retained.

(d) Warm-blooded animals, adult reptiles, and adult terrestrial amphibians used in laboratory procedures that require manipulations and observations over an extended period of time or in studies that require these test systems to be removed from and returned to their test system-housing units for any reason (e.g., cage cleaning, treatment, etc.), shall receive appropriate identification (e.g., tattoo, toe clip, color code, ear tag, ear punch, etc.). All information needed to specifically identify each test system within the test system-housing unit shall appear on the outside of that unit. Suckling mammals and juvenile birds are excluded from the requirement of individual identification unless otherwise specified in the protocol.

(e) Except as specified in paragraph (e)(1) of this section, test systems of different species shall be housed in separate rooms when necessary. Test systems of the same species, but used in different studies, should not ordinarily be housed in the same room when inadvertent exposure to test, control, or reference substances or test system mixup could affect the outcome of either study. If such mixed housing is necessary, adequate differentiation by space and identification shall be made.

(1) Plants, invertebrate animals, aquatic vertebrate animals, and organisms that may be used in multispecies tests need not be housed in separate rooms, provided that they are adequately segregated to avoid mixup and cross contamination.

(2) [Reserved]

(f) Cages, racks, pens, enclosures, aquaria, holding tanks, ponds, growth chambers, and other holding, rearing, and breeding areas, and accessory equipment, shall be cleaned and sanitized at appropriate intervals.

(g) Feed, soil, and water used for the test systems shall be analyzed periodically to ensure that contaminants known to be capable of interfering with the study and reasonably expected to be present in such feed, soil, or water are not present at levels above those specified in the protocol. Documentation of such analyses shall be maintained as raw data.

(h) Bedding used in animal cages or pens shall not interfere with the purpose or conduct of the study and shall be changed as often as necessary to keep the animals dry and clean.

(i) If any pest control materials are used, the use shall be documented. Cleaning and pest control materials that interfere with the study shall not be used.

(j) All plant and animal test organisms shall be acclimatized, prior to their use in an experiment, to the environmental conditions of the test.

Subpart F—Test, Control, and Reference Substances

19. By revising the heading for Subpart F to read as set forth above.

20. By revising § 792.105 to read as follows:

§ 792.105 Test, control and reference substance characterization.

(a) The identity, strength, purity, and composition, or other characteristics which will appropriately define the test, control, or reference substance shall be determined for each batch and shall be documented before its use in an experiment. Methods of synthesis, fabrication, or derivation of the test, control, or reference substance shall be documented by the sponsor or the testing facility.

(b) The stability and, when relevant to the conduct of the experiment, the solubility of each test, control, or reference substance shall be determined by the testing facility or by the sponsor before the experimental start date. Where periodic analysis of each batch is required by the protocol, there shall be written standard operating procedures that shall be followed.

(c) Each storage container for a test, control, or reference substance shall be labeled by name, chemical abstracts service number (CAS) or code number, batch number, expiration date, if any, and, where appropriate, storage conditions necessary to maintain the

identity, strength, purity, and composition of the test, control, or reference substance. Storage containers shall be assigned to a particular test substance for the duration of the study.

(d) For studies of more than 4 weeks' duration, reserve samples from each batch of test, control, and reference substances shall be retained for the period of time provided by § 792.195.

(e) The stability of test, control, and reference substances under test conditions shall be known for all studies.

21. In § 792.107, by revising the section heading and introductory text to read as follows:

§ 792.107 Test, control, and reference substance handling.

Procedures shall be established for a system for the handling of the test, control, and reference substances to ensure that:

* * * * *

22. By revising § 792.113 to read as follows:

§ 792.113 Mixtures of substances with carriers.

(a) For each test, control, or reference substance that is mixed with a carrier, tests by appropriate analytical methods shall be conducted:

(1) To determine the uniformity of the mixture and to determine, periodically, the concentration of the test, control, or reference substance in the mixture.

(2) To determine the stability and, when relevant to the conduct of the experiment, the solubility of the test, control, or reference substance in the mixture, before the experimental start date. Determination of the stability and solubility of the test, control, or reference substance in the mixture shall be done under the environmental conditions specified in the protocol and as required by the conditions of the experiment. Where periodic analysis of the mixture is required by the protocol, there shall be written standard operating procedures that shall be followed.

(b) Where any of the components of the test, control, or reference substance carrier mixture has an expiration date, that date shall be clearly shown on the container. If more than one component has an expiration date, the earliest date shall be shown.

(c) If a vehicle is used to facilitate the mixing of a test substance with a carrier, assurance shall be provided that the vehicle does not interfere with the integrity of the test.

23. In § 792.120, by revising paragraph (a) to read as follows:

§ 792.120 Protocol.

(a) Each study shall have an approved written protocol that clearly indicates the objectives and all methods for the conduct of the study. The protocol shall contain but shall not necessarily be limited to the following information:

(1) A descriptive title and statement of the purpose of the study.

(2) Identification of the test, control, and reference substance by name, chemical abstracts service (CAS) number or code number.

(3) The name and address of the sponsor and the name and address of the testing facility at which the study is being conducted.

(4) The proposed experimental start and termination dates.

(5) Justification for selection of the test system.

(6) Where applicable, the number, body weight, sex, source of supply, species, strain, substrain, and age of the test system.

(7) The procedure for identification of the test system.

(8) A description of the experimental design, including methods for the control of bias.

(9) Where applicable, a description and/or identification of the diet used in the study as well as solvents, emulsifiers and/or other materials used to solubilize or suspend the test, control, or reference substances before mixing with the carrier. The description shall include specifications for acceptable levels of contaminants that are reasonably expected to be present in the dietary materials and are known to be capable of interfering with the purpose or conduct of the study if present at levels greater than established by the specifications.

(10) The route of administration and the reason for its choice.

(11) Each dosage level, expressed in milligrams per kilogram of body or test system weight or other appropriate units, of the test, control, or reference substance to be administered and the method of frequency of administration.

(12) The type and frequency of test analyses, and measurements to be made.

(13) The records to be maintained.

(14) The date of approval of the protocol by the sponsor and the dated signature of the study director.

(15) A statement of the proposed statistical method.

* * * * *

24. In § 792.130, by revising paragraphs (d) and (e) to read as follows:

§ 792.130 Conduct of a study.

* * * * *

(d) In animal studies where histopathology is required, records of gross findings for a specimen from postmortem observations shall be available to a pathologist when examining that specimen histopathologically.

(e) All data generated during the conduct of a study, except those that are generated by automated data collection systems, shall be recorded directly, promptly, and legibly in ink. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data. Any change in entries shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of the change. In automated data collection systems, the individual responsible for direct data input shall be identified at the time of data input. Any change in automated data entries shall be made so as not to obscure the original entry, shall indicate the reason for change, shall be dated, and the responsible individual shall be identified.

25. By adding § 792.135 to read as follows:

§ 792.135 Physical and chemical characterization studies.

(a) Except as provided in paragraph (b) of this section, the following provisions shall not apply to studies designed to determine physical and chemical characteristics of a test, control, or reference substance:

§ 792.31 (c), (d), and (g)
§ 792.35 (b) and (c)
§ 792.43
§ 792.45
§ 792.47
§ 792.49
§ 792.81(b) (1), (2), (6) through (9), and (12)
§ 792.90
§ 792.105 (a) through (d)
§ 792.113
§ 792.120(a) (5) through (12), and (15)
§ 792.185(a) (5) through (8), (10), (12), and (14)
§ 792.195 (c) and (d).

(b) The exemptions provided in paragraph (a) of this section shall not apply to physical/chemical characterization studies designed to determine solubility, octanol water partition coefficient, volatility, and persistence (such as biodegradation, photodegradation, and chemical degradation studies), and such studies shall be conducted in accordance with this part.

26. In § 792.185, by revising paragraphs (a) (4) and (5) to read as follows:

§ 792.185 Reporting of study results.

(a) * * *

(4) The test, control, and reference substances identified by name, chemical abstracts service (CAS) number or code number, strength, purity, and composition, or other appropriate characteristics.

(5) Stability and, when relevant to the conduct of the experiment, the solubility of the test, control, and reference substances under the conditions of administration.

* * * * *

27. In § 792.190, by revising paragraphs (a) and (e) to read as follows:

§ 792.190 Storage and retrieval of records and data.

(a) All raw data, documentation, records, protocols, specimens, and final reports generated as a result of a study shall be retained. Specimens obtained from mutagenicity tests, specimens of soil, water, and plants, and wet specimens of blood, urine, feces, and biological fluids, do not need to be retained beyond quality assurance review. Correspondence and other documents relating to interpretation and evaluation of data, other than those documents contained in the final report, also shall be retained.

* * * * *

(e) Material retained or referred to in the archives shall be indexed to permit expedient retrieval.

28. In § 792.195, by revising paragraphs (b) and (c), and adding paragraph (i), to read as follows:

§ 792.195 Retention of records.

* * * * *

(b) Except as provided in paragraph (c) of this section, documentation records, raw data, and specimens pertaining to a study and required to be retained by this part shall be retained in the archive(s) for a period of at least 5 years following the date on which the results of the study are submitted to EPA.

(c) Wet specimens, samples of test, control, or reference substances, and specially prepared material, which are relatively fragile and differ markedly in stability and quality during storage, shall be retained only as long the quality of the preparation affords evaluation. Specimens obtained from mutagenicity tests, specimens of soil, water, and plants, and wet specimens of blood, urine, feces, biological fluids, do not need to be retained beyond quality assurance review. In no case shall retention be required for longer periods than those set forth in paragraph (b) of this section.

* * * * *

(i) Records required by this part may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records.

Subpart L—[Removed]

29. By removing Subpart L—*Environmental Testing Provisions,* consisting of §§ 792.225, 792.226, 792.228, and 792.232.

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